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Supplementation of trehalulose in stingless bee honey improved glucose tolerance and insulin sensitivity in Type 2 Diabetic-induced rats *In Vivo*

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Abstract

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Hyperglycemia is defined as excessive blood glucose levels and often leads to a diagnosis of type 2 diabetes. Trehalulose, a rare disaccharide with a low glycemic index, was recently discovered to be a unique major bioactive component in stingless bee honey (SBH), produced alongside the regular disaccharides fructose and glucose [1]. Although traditionally, SBH is being used for the prevention of type 2 diabetes, currently, there are no available clinical studies correlating the effects. Therefore, this study was conducted to investigate the subacute and sub-chronic antidiabetic effects of trehalulose-rich SBH (TRSBH) consisting of 56% trehalulose in a non-diabetic and type 2 diabetic-induced (T2DI) Sprague-Dawley rat model.

The sample SBH produced by *G. thoracica* species were collected and pooled multiple times from Ladang 10, Universiti Putra Malaysia (UPM) (2°59'28.7"N, 101°42'52.9"E), between 2022 and 2023. Fifty-four female Sprague Dawley rats (age: 5-7 weeks age, body weight: 200 ± 20 g) were used for both subacute (28 days) and sub-chronic (60 days) anti-diabetic studies of TRSBH. Non-treated group and metformin-treated group (300mg/kg) were used as Controls. The TRSBH were supplemented at 1.0, 1.5, and 2.0 g/kg bodyweight for 28 days. Glucose area under the curve (AUC) and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) were calculated as glucose tolerance and insulin sensitivity indices, respectively.

Subacute supplementation showed no significant ($P>0.05$) effects on body weight, normal rats' fasting blood glucose, insulin, or HOMA-IR. However, sub-chronic 60 days treatment at 1.0 g/kg body weight and 2.0 g/kg bodyweight trehalulose in SBH on T2DI rats were found to significantly ($P<0.05$) prevented hyperinsulinemia, improved glucose tolerance and insulin sensitivity comparable to the effects observed in the metformin-treated group and notably more significant ($P<0.05$) than the diabetic control rats. The T2DI rats were supplemented with 2.0 g/kg b.w. trehalulose in SBH exhibited significantly ($P<0.05$) lower fasting insulin levels (0.18 ± 0.01 ng/mL) than the diabetic control rats (0.29 ± 0.01 ng/mL). No toxicity effects were observed based on histopathological tests.

Our study is the first to demonstrate the dose-response effects of TRSBH supplementation *in vivo*. Sub-chronic supplementation of TRSBH for 60 days at low and moderate doses prevented hyperinsulinemia and induced significantly ($P<0.05$) improved glucose tolerance and insulin sensitivity in diabetic-induced rats comparable to the metformin-treated group. As a dietary supplement, a trehalulose dose of up to 2.0 g/kg bodyweight in SBH can benefit blood glucose and insulin regulation. In conclusion, although the current dietary guidelines for disaccharide intake in the daily diet are similar for all types, these findings suggest that the guidelines may need to be set explicitly for different types of disaccharides. However, further clinical investigation on the impact of its' long-term consumption using randomized-control trials in humans should be conducted before drawing the guidelines.

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